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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,608	01/06/2006	Hasan Kulaksiz	26605.00001	7597

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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
01/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,608	KULAKSIZ ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/12/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *2,5-15 and 17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,15,16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05/19/05* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I claims 1, 3, 4, 15 and 16 in the reply filed on December 12, 2007 is acknowledged.

Drawings

The subject matter of this application admits of illustration by a drawing to facilitate understanding of the invention. Applicant is required to furnish a drawing under 37 CFR 1.81(c). No new matter may be introduced in the required drawing. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). The specification on page 7, lines 4-9 make reference to Figures 6-9 for understanding the current invention. Also, pages 49-50 make reference to Figure 7. However, there are no Figures 6-9 in the current application. A review of the drawings submitted May 19, 2005 indicates that Figures 1-5 and 10-16 were submitted. However, there are no Figures 6-9 listed in these drawings.

Specification

2. The disclosure is objected to because of the following informalities: The current specification makes reference to Figures 6-9 (see for example, Pages 7, 49 and 50). However, there are no Figures 6-9 in the application.

3. The disclosure is also objected to because Figure 1 discloses "Pro-Hepcidin(aa25-94)". This should be –Pro-Hepcidin(aa25-84)--. If applicant corrects the drawing, applicant is reminded that each drawing sheet submitted after the filing date of

an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification on page 55 discloses that Although, the C-terminal antibody EG(1)-HepC revealed specific results in dot blot, Western blot, immnohistochemistry and immunofluorescence experiments, no immunoreactivity could be obtained in ELISA. The compact folding pattern of hepcidin and its tertiary structure in blood may account for the inability of the EG(1) - HepC antibody to identify circulating hepcidin. Thus, the specification is teaching that the antibody does not work in blood samples with an ELISA assay. The specification does not teach an antibody which specifically binds to a carboxy terminal epitope of SEQ ID NO:2 and is quantified by conducting an ELISA assay.

6. Claims 1, 3, 4, 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tissue samples of liver and kidney

and a urine sample, does not reasonably provide enablement for any and all samples as broadly recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for diagnosing a disease condition characterized by non-physiological levels of hepcidin, comprising obtaining a tissue or fluid sample from a subject; contacting the sample with an antibody or fragment thereof that specifically binds to one or more carboxy terminal epitopes of SEQ ID NO: 2 and quantifying hepcidin level in the sample; wherein the non-physiological level of hepcidin is indicative of the disease condition.

The specification fails to teach obtaining any and all tissue or fluid samples from a subject and utilizing an antibody which specifically binds to one or more carboxy terminal epitopes of SEQ ID NO: 2 and quantifying hepcidin in the sample and diagnosing a disease condition. The specification on pages 6-9 disclose obtaining

kidney and urine samples from a subject and detecting hepcidin with the antibody EG(1) - HepC which specifically binds the carboxy terminal epitope of SEQ ID NO: 2. Also, Figure 2 shows that this antibody is not reactive in human serum. Page 7 discloses that the EG(1) - HepC antibody is reactive with liver and urine sample. Page 70 also discloses liver and kidney samples. Page 55 of the specification specifically teaches that C-terminal antibody EG(1)-HepC was reactive in dot blot, Western blot, immunohitochemistry and immunofluorescence experiments (Figures 1-4) (note that Figures 1-4 only teach the samples are kidney and urine samples), no immunoreactivity could be obtained in ELISA. The compact folding pattern of hepcidin and its tertiary structure in the blood may account for the inability of the EG(1) - HepC antibody to identify circulating hepcidin. Thus, it appears that the disclosure is teaching that the EG(1) - HepC antibody does not detect hepcidin in blood, serum or plasma. Also, Swinkels et al (Clinical Chemistry 52, No. 6, 2006, pages 950-968) teaches that for serum samples only the measurement of prohepcidin is possible, by a commercially available ELISA that uses antibodies directed against amino acid residues 28-47 (N-terminal)(p. 961 2nd col). The specification does not show or teach samples such as tears, semen, plasma, serum, blood, brain tissue, lung tissue etc,. that can or could be used in methods of diagnosing as recited nor does the specification teach or show that antibodies which specifically bind to the carboxy terminal epitopes of SEQ ID NO: 2 can detect hepcidin in these samples and as shown above the specification actually teaches that it does not work in samples of blood, serum or plasma. Further, antibodies which specifically bind to the carboxy terminal epitope of hepcidin are not well known in the

art. There are no working examples in the specification directed to serum, blood, tears, semen, brain tissue etc. The examples of the specification are limited to kidney tissue, liver tissue and urine. Thus, one of skill in the art cannot practice the invention without undue experimentation because of the number of fluid samples that can be tested (i.e. tear, csf, sputum, saliva, blood, serum, plasma, embryonic fluid, brain tissue, lung tissue etc.) and the lack of predictability that these fluids contain hepcidin and further that if it were to contain hepcidin that the hepcidin would be reactive with the antibody.

7. Claims 1, 3, 4, 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hereditary hemochromatosis, chronic renal insufficiency and renal anemia, does not reasonably provide enablement for any and all disease conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for diagnosing a disease condition characterized by non-physiological levels of hepcidin, comprising obtaining a tissue or fluid sample from a subject; contacting the sample with an antibody or fragment thereof that specifically binds to one or more carboxy terminal epitopes of SEQ ID NO: 2 and quantifying hepcidin level in the sample; wherein the non-physiological level of hepcidin is indicative of the disease condition.

The specification fails to teach diagnosing any and all disease conditions using the instantly recited methods. The specification on page 49, line 21- page 50 line 28 discloses the pro-hepcidin levels in hereditary hemochromatosis, chronic renal insufficiency and renal anemia as compared to healthy control groups and shows a correlation of these levels with the disease as compared to the healthy control groups. Swinkels et al (Clinical Chemistry 52:6 pages 950-968, 2006) teaches that it is not well known of assays for detection and determining the levels of hepcidin. Swinkels teaches that detection and quantification in plasma or urine have not been widely available, and the development of reagents has been hampered by technical difficulties (p. 961, 2nd col). Swinkels also teaches that levels of hepcidin correlate with Hereditary Hemochromatosis and does not teach that it correlates with any and all diseases or disease conditions. The only examples in the specification correlating levels of hepcidin with disease are directed to hepcidin levels in hereditary hemochromatosis, chronic renal insufficiency and renal anemia. Further, as indicated above the detection of levels of hepcidin and correlation of levels with disease is not well known in the art. At best the quantification of hepcidin as compared to controls can only be used for diagnosis of

hereditary hemochromatosis, chronic renal insufficiency and renal anemia. Therefore, such is not seen as sufficient to support any and all disease conditions and as set forth below it is unclear what is considered to be disease condition and one skilled in the art cannot practice the claimed invention without undue experimentation because if hepcidin is not known to be associated with any and all disease conditions one cannot positively diagnose the disease without undue experimentation.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 3, 4, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 1 the recitation "disease condition" is vague and indefinite. It is unclear what is considered to be a disease condition. Does applicant intend the actual disease or does applicant intend a condition of a disease such as fever, weight loss, and plaque build up or does applicant intend something else. There is no definition provided for the term in the specification and it is unclear what applicant is trying to encompass.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1, 3, 4, 15 and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4 of copending Application No. 10/299,486. Although the conflicting claims are not identical, they are not patentably distinct from each other because one of both applications are directed to determining levels of hepcidin in a sample of the subject with an antibody which specifically binds to one or more carboxy epitopes of hepcidin and one of skill would recognize that the claims of copending application 10/299,486 would encompass the currently recited claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit 1641
January 16, 2008

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